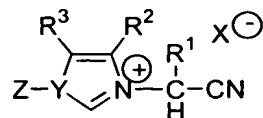


What is claimed:

1. A compound of the formula:



5 wherein :

Y is N or S;

Z is absent when Y is S and, if present, Z is an alkyl group of 1 to 7 carbon atoms, vinyl, allyl, arylcarbonyl, amino or alkoxycarbonylalkyl, or Z is according to the formula  $-\text{CH}(\text{R}^4)(\text{CN})$ , or Z is  $-\text{CH}_2\text{C}(=\text{O})\text{R}^5$ , where  $\text{R}^5$  is (a) a  $\text{C}_6$ - $\text{C}_{10}$  aryl group, said aryl group optionally substituted by one or more alkyl, alkoxy, halo, dialkylamino, hydroxy, nitro or  $\text{C}_1$ - $\text{C}_2$  alkylenedioxy groups or (b) heterocyclic group containing 4-10 ring members and 1-3 heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur wherein the heterocyclic group can be substituted by one or more substituents selected from the group consisting of alkyl, oxo, alkoxycarbonylalkyl, aryl, and aralkyl group, and the one or more substituents can be substituted by one or more alkyl or alkoxy groups,

$\text{R}^1$  and  $\text{R}^4$  are independently hydrogen, alkyl or phenyl optionally substituted with one or more halogen, alkyl, di(lower alkyl)amino or alkoxy groups; and

$\text{R}^2$  and  $\text{R}^3$  are:

1. independently selected from hydrogen, acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino,  $(\text{C}_1$ - $\text{C}_3)$ alkylenedioxy, allyl, amino,  $\omega$ -alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo, hydroxy,  $(\text{C}_2$ - $\text{C}_6)$ hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, alkylsulfonyl, alkylsulfinyl, alkylthio, trifluoromethyl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, 4- $[\text{C}_6$  or  $\text{C}_{10}]$ arylpiperidin-1-yl, 4- $[\text{C}_6$  or  $\text{C}_{10}]$ arylpiperazin-1-yl, Ar {wherein, consistent with the rules of aromaticity, Ar is  $\text{C}_6$  or  $\text{C}_{10}$  aryl or a 5- or 6-membered heteroaryl ring, wherein 6-

*Subar*  
5

0505035.071301

membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, each heteroaryl ring can be fused to a benzene, pyridine, pyrimidine, pyridazine, pyrazine, or (1,2,3)triazine (wherein the ring fusion is at a carbon-carbon double bond of Ar)}, Ar-alkyl, Ar-O, ArSO<sub>2</sub>-, ArSO-, ArS-, ArSO<sub>2</sub>NH-, ArNH, (N-Ar)(N-alkyl)N-, ArC(O)-, ArC(O)NH-, ArNH-C(O)-, and (N-Ar)(N-alkyl)N-C(O)-, or together R<sub>1</sub> and R<sub>2</sub> comprise methylenedioxy; or

2. together with their ring carbons form a C<sub>6</sub>- or C<sub>10</sub>- aromatic fused ring system; or
3. together with their ring carbons form a C<sub>5</sub>-C<sub>7</sub> fused cycloalkyl ring having up to two double bonds including the fused double bond of the -olium or -onium containing ring, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl, alkoxycarbonyl, amino, aminocarbonyl, carboxy, fluoro, or oxo substituents; or
4. together with their ring carbons form a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, each heteroaryl ring may be optionally substituted with one or more 1-pyrrolidinyl-, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperazin-1-yl, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, halo or (C<sub>1</sub>-C<sub>3</sub>)alkylenedioxy groups; or
5. together with their ring carbons form a five to eight membered heterocycle, wherein the heterocycle consists of ring atoms selected from the group consisting of carbon, nitrogen, and S(O)<sub>n</sub>, where n=0,1, or 2; and X<sup>-</sup> is a biologically or pharmaceutically acceptable anion,

wherein aryl or Ar can be substituted with, in addition to any substitutions specifically noted, one or more substituents selected from the group consisting of acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, (C<sub>1</sub>-C<sub>3</sub>)alkylenedioxy, alkylsulfonyl, alkylsulfinyl, ω-alkylenesulfonic acid, alkylthio, allyl, amino, ArC(O)-,

ArC(O)NH-, ArO-, Ar-, Ar-alkyl-, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo, trifluoromethyl, hydroxy, (C<sub>2</sub>-C<sub>6</sub>)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, 1-pyrrolidinyl, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperazin-1-yl-, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl; and

wherein heterocycles, except those of Ar, can be substituted with, in addition to any substitutions specifically noted, acylamino, alkanoyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, alkylsulfonyl, alkylsulfinyl, alkylthio, amino, ArC(O)-, ArO-, Ar-, carboxy, dialkylamino, fluoro, fluoroalkyl, difluoroalkyl, hydroxy, mercapto, sulfamoyl, or trifluoromethyl.

2. The compound of claim 1, wherein R<sup>2</sup> and R<sup>3</sup> are independently hydrogen, alkyl, or together form an alkylene bridge of 3-4 carbon atoms.

3. The compound of claim 1, wherein R<sup>1</sup> is hydrogen.

4. The compound of claim 1, wherein Z is an alkyl group of 1 to 7 carbon atoms.

5. The compound of claim 3, wherein Z is C<sub>1</sub> to C<sub>3</sub> alkyl.

6. The compound of claim 4, wherein R is hydrogen.

7. The compound of claim 1, wherein is an alkyl group of 1 to 7 carbon atoms, arylcarbonyl, amino or alkoxycarbonylalkyl, or Z is according to the formula -CH(R<sup>4</sup>)(CN), or Z is -CH<sub>2</sub>C(=O)R<sup>5</sup>, where R<sup>5</sup> is a C<sub>6</sub>-C<sub>10</sub> aryl group, said aryl group optionally substituted by one or more alkyl, alkoxy, halo, dialkylamino, hydroxy, nitro or C<sub>1</sub>-C<sub>2</sub> alkylendioxy groups.

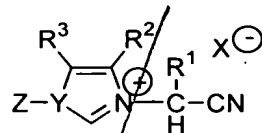
8. The compound of claim 1, wherein Z is an alkyl group of 1 to 7 carbon atoms, arylcarbonyl, amino or alkoxycarbonylalkyl, or Z is according to the formula -CH(R<sup>4</sup>)(CN).

9. A compound of the formula:

0690503.074304

*Sub A 2*

*Sub A 3*



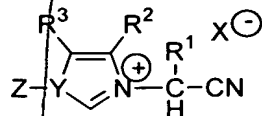
wherein :

Y is N or S;

- 5 Z is absent when Y is S and, if present, Z is an alkyl group of 1 to 7 carbon atoms, arylcarbonyl, amino or (lower)alkoxycarbonyl(lower)alkyl, or Z is according to the formula  $\text{CH}(\text{R}^4)(\text{CN})$ , or Z is  $-\text{CH}_2\text{C}(=\text{O})\text{R}^5$ , where  $\text{R}^5$  is (a) a  $\text{C}_6\text{-C}_{10}$  aryl group, said aryl group optionally substituted by one or more lower alkyl, lower alkoxy, halo, di(lower)alkylamino, hydroxy, nitro or  $\text{C}_1\text{-C}_2$  alkylenedioxy groups or (b) heterocyclic group containing 4-10 ring members and 1-3 heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur wherein the heterocyclic group can be substituted by one or more substituents selected from the group consisting of alkyl, oxo, alkoxycarbonylalkyl, aryl, and aralkyl group, and the one or more substituents can be substituted by one or more alkyl or alkoxy groups,
- 15  $\text{R}^1$  and  $\text{R}^4$  are independently hydrogen, lower alkyl or phenyl optionally substituted with one or more halogen, lower alkyl, di(lower alkyl)amino or alkoxy groups;
- 20  $\text{R}^2$  and  $\text{R}^3$  are independently hydrogen, lower alkyl, or together form an alkylene bridge of 3-4 carbon atoms; and
- $\text{X}^-$  is a biologically or pharmaceutically acceptable anion.

- 25 **10.** A method of, in an animal, (i) improving the elasticity or reducing wrinkles of a skin, treating (ii) diabetes or treating, inhibiting the (iii) discoloration of teeth, or ameliorating one or more of the following conditions: (iv) adverse sequelae of diabetes, (v) kidney damage, (vi) damage to blood vasculature, (vii) hypertension, (viii) retinopathy, (ix) damage to lens proteins, (x) cataracts, (xi) peripheral neuropathy, (xii) osteoarthritis, or (xiii) damage to cardiovascular tissue due to heart failure, (xiv)
- 30 improving myocardial elasticity, (xv) preventing damage to tissues in the intraperitoneal

cavity caused by contact with elevated levels of reducing sugars, or (xvi) treating or ameliorating one of the conditions described above, the method comprising administering an effective amount of one or more compounds of the formula:



5 wherein :

Y is N or S;

Z is absent when Y is S and, if present, Z is an alkyl group of 1 to 7 carbon atoms, vinyl, allyl, arylcarbonyl, amino or alkoxycarbonylalkyl, or Z is according to the formula  $-\text{CH}(\text{R}^4)(\text{CN})$ , or Z is  $-\text{CH}_2\text{C}(=\text{O})\text{R}^5$ , where  $\text{R}^5$  is (a) a  $\text{C}_6$ - $\text{C}_{10}$  aryl group, said aryl group optionally substituted by one or more alkyl, alkoxy, halo, dialkylamino, hydroxy, nitro or  $\text{C}_1$ - $\text{C}_2$  alkylenedioxy groups or (b) heterocyclic group containing 4-10 ring members and 1-3 heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur wherein the heterocyclic group can be substituted by one or more substituents selected from the group consisting of alkyl, oxo, alkoxycarbonylalkyl, aryl, and aralkyl group, and the one or more substituents can be substituted by one or more alkyl or alkoxy groups,  $\text{R}^1$  and  $\text{R}^4$  are independently hydrogen, alkyl or phenyl optionally substituted with one or more halogen, alkyl, di(lower alkyl)amino or alkoxy groups; and

$\text{R}^2$  and  $\text{R}^3$  are:

1. independently selected from hydrogen, acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino,  $(\text{C}_1$ - $\text{C}_3)$  alkylenedioxy, allyl, amino,  $\omega$ -alkylenesulfonic acid, carbamoyl, carboxy, carboxyalkyl, cycloalkyl, dialkylamino, halo, hydroxy,  $(\text{C}_2$ - $\text{C}_6)$  hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, alkylsulfonyl, alkylsulfinyl, alkylthio, trifluoromethyl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, 4- $[\text{C}_6$  or  $\text{C}_{10}]$  arylpiperidin-1-yl, 4- $[\text{C}_6$  or  $\text{C}_{10}]$  arylpiperazin-1-yl, Ar {wherein, consistent with the rules of aromaticity, Ar is  $\text{C}_6$  or  $\text{C}_{10}$  aryl or a 5- or 6-membered heteroaryl ring, wherein 6-membered heteroaryl ring contains one to three atoms of N, and the 5-

membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, each heteroaryl ring can be fused to a benzene, pyridine, pyrimidine, pyridazine, pyrazine, or (1,2,3)triazine (wherein the ring fusion is at a carbon-carbon double bond of Ar)}, Ar-alkyl, Ar-O, ArSO<sub>2</sub>-, ArSO-, ArS-, ArSO<sub>2</sub>NH-, ArNH, (N-Ar)(N-alkyl)N-, ArC(O)-, ArC(O)NH-, ArNH-C(O)-, and (N-Ar)(N-alkyl)N-C(O)-, or together R<sub>1</sub> and R<sub>2</sub> comprise methylenedioxy; or

2. together with their ring carbons form a C<sub>6</sub>- or C<sub>10</sub>- aromatic fused ring system; or

3. together with their ring carbons form a C<sub>5</sub>-C<sub>7</sub> fused cycloalkyl ring having up to two double bonds including the fused double bond of the -olium or -onium containing ring, which cycloalkyl ring can be substituted by one or more of the group consisting of alkyl, alkoxy carbonyl, amino, aminocarbonyl, carboxy, fluoro, or oxo substituents; or

4. together with their ring carbons form a 5- or 6-membered heteroaryl ring, wherein the 6-membered heteroaryl ring contains one to three atoms of N, and the 5-membered heteroaryl ring contains from one to three atoms of N or one atom of O or S and zero to two atoms of N, each heteroaryl ring may be optionally substituted with one or more 1-pyrrolidinyl-, 4-[C<sub>6</sub> or C<sub>10</sub>]aryl piperazin-1-yl, 4-[C<sub>6</sub> or C<sub>10</sub>]aryl piperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl, halo or (C<sub>1</sub>-C<sub>3</sub>)alkylenedioxy groups; or

5. together with their ring carbons form a five to eight membered heterocycle, wherein the heterocycle consists of ring atoms selected from the group consisting of carbon, nitrogen, and S(O)<sub>n</sub>, where n=0,1, or 2; and

X<sup>-</sup> is a biologically or pharmaceutically acceptable anion,

wherein aryl or Ar can be substituted with, in addition to any substitutions specifically noted, one or more substituents selected from the group consisting of acylamino, acyloxyalkyl, alkanoyl, alkanoylalkyl, alkenyl, alkoxy, alkoxy carbonyl, alkoxy carbonylalkyl, alkyl, alkylamino, (C<sub>1</sub>-C<sub>3</sub>)alkylenedioxy, alkylsulfonyl, alkylsulfinyl, ω-alkylenesulfonic acid, alkylthio, allyl, amino, ArC(O)-, ArC(O)NH-, ArO-, Ar-, Ar-alkyl-, carboxy, carboxyalkyl, cycloalkyl,

dialkylamino, halo, trifluoromethyl, hydroxy, (C<sub>2</sub>-C<sub>6</sub>)hydroxyalkyl, mercapto, nitro, sulfamoyl, sulfonic acid, 1-pyrrolidinyl, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperazin-1-yl-, 4-[C<sub>6</sub> or C<sub>10</sub>]arylpiperidin-1-yl, azetidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, piperidin-1-yl; and

- 5 wherein heterocycles, except those of Ar, can be substituted with, in addition to any substitutions specifically noted, acylamino, alkanoyl, alkoxy, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylamino, alkylsulfonyl, alkylsulfinyl, alkylthio, amino, ArC(O)-, ArO-, Ar-, carboxy, dialkylamino, fluoro, fluoroalkyl, difluoroalkyl, hydroxy, mercapto, sulfamoyl, or trifluoromethyl.

10

11. The method of claim 8, comprising administering an effective amount of one or more of the compounds wherein R<sup>1</sup> is hydrogen.

12. The method of claim 8, comprising administering an effective amount of one or more of the compounds wherein Z is an alkyl group of 1 to 7 carbon atoms.

15

13. The method of claim 8, comprising administering an effective amount of one or more of the compounds wherein Z is C<sub>1</sub> to C<sub>3</sub> alkyl.

14. The method of claim 11, comprising administering an effective amount of one or more of the compounds wherein R is hydrogen.

20

15. The method of claim 11, comprising administering an effective amount of one or more of the compounds wherein Z is an alkyl group of 1 to 7 carbon atoms, arylcarbonyl, amino or alkoxycarbonylalkyl, or Z is according to the formula -

25

CH(R<sup>4</sup>)(CN), or Z is -CH<sub>2</sub>C(=O)R<sup>5</sup>, where R<sup>5</sup> is a C<sub>6</sub>-C<sub>10</sub> aryl group, said aryl group optionally substituted by one or more alkyl, alkoxy, halo, dialkylamino, hydroxy, nitro or C<sub>1</sub>-C<sub>2</sub> alkylenedioxy groups.

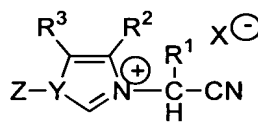
16. The method of claim 7, wherein Z is an alkyl group of 1 to 7 carbon atoms, arylcarbonyl, amino or alkoxycarbonylalkyl, or Z is according to the formula -

30

CH(R<sup>4</sup>)(CN).

17. The method of claim 7, comprising administering an effective amount of the one or more compounds to improve myocardial elasticity or reduce any loss of myocardial elasticity in heart failure.

18. A method of, in an animal, (i) improving the elasticity or reducing wrinkles of a skin, treating (ii) diabetes or treating, inhibiting the (iii) discoloration of teeth, or ameliorating one or more of the following conditions: (iv) adverse sequelae of diabetes, (v) kidney damage, (vi) damage to blood vasculature, (vii) hypertension, (viii) retinopathy, (ix) damage to lens proteins, (x) cataracts, (xi) peripheral neuropathy, (xii) osteoarthritis, or (xiii) damage to cardiovascular tissue due to heart failure, (xiv) improving myocardial elasticity, (xv) preventing damage to tissues in the intraperitoneal cavity caused by contact with elevated levels of reducing sugars, or (xvi) treating or ameliorating one of the conditions described above, the method comprising administering an effective amount of one or more compounds of the formula:



wherein:

Y is N or S;

Z is absent when Y is S and, if present, Z is an alkyl group of 1 to 7 carbon atoms, arylcarbonyl, amino or (lower)alkoxycarbonyl(lower)alkyl, or Z is according to the formula  $-\text{CH}(\text{R}^4)(\text{CN})$ , or Z is  $-\text{CH}_2\text{C}(=\text{O})\text{R}^5$ , where  $\text{R}^5$  is (a) a  $\text{C}_6\text{-C}_{10}$  aryl group, said aryl group optionally substituted by one or more lower alkyl, lower alkoxy, halo, di(lower)alkylamino, hydroxy, nitro or  $\text{C}_1\text{-C}_2$  alkylendioxy groups or (b) heterocyclic group containing 4-10 ring members and 1-3 heteroatoms selected from the group consisting of oxygen, nitrogen and sulfur wherein the heterocyclic group can be substituted by one or more substituents selected from the group consisting of alkyl, oxo, alkoxycarbonylalkyl, aryl, and aralkyl group, and the one or more substituents can be substituted by one or more alkyl or alkoxy groups,



~~$R^4$  are independent  
substituted with  
or alkoxy groups  
 $R^3$  are independent  
bridge of 3-4  
biologically~~

X<sup>-</sup> is a biologically or pharmaceutically acceptable anion.

5

05906036 "071311